The use of CO2 removal devices in patients awaiting lung transplantation: an initial experience.

Pre-transplant extracorporeal decapneization devices: a single center initial experience

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Keywords:

Abstract:words

Text: words

Tables:

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Abstract

Background

Lung transplantation is the treatment of choice for patients with end-stage lung failure. The most important limitations are represented by the shortage of donors and the too long period on waiting list. New techniques such as extracorporeal membrane ventilator devices with or without pump support have been developed as bridge to transplant for those patients with severe unresponsive respiratory insufficiency.

Methods

Between November 2005 and September 2009, 12 patients (7 male and 5 female; mean age 43.3 ± 15.5 years) underwent decapneization with extracorporeal devices. In 6 cases a NovaLung system has been used while in the remaining 6 patients a Decap device has been applied. The causes of respiratory failure that led to the implantation of such devices were: cystic fibrosis (6 pts), pulmonary emphysema (4 pts), obliterant bronchiolitis (1 pts) and one case of chronic rejection in a previous double lung transplantation

Results

Mean time on extracorporeal decapneization has been 13.5 ± 14.2 days. 8/12 patients (67%) died on device. In 3 cases patients were bridged to lung transplantation, while 1 patient recovered from the acute phase and was weaned from the device after 11 days. Mean PaCO2 on extracorporeal gas exchange has been significantly lower for both the devices at 24, 48 and 72 hours after assistance implantation ($p<0.05$). No statistical difference has been observed for both the systems used.

Conclusions

In our initial experience the decapneization devices used have been simple and efficient methods to support patients with mild hypoxia and severe hypercapnia refractory to mechanical ventilation. This could represent a valid bridge to lung transplant in such patients. The limited number of available donors remains a problem especially for patients on extracorporeal assistance.

Introduction

The number of patients listed for lung transplantation (Ltx) is continuously rising. Even if lung transplant procedures are annually increasing the number of patients waiting for LTx still overcomes the number of available grafts [1]. The need for alternative solutions as bridge to transplants or to recovery,

especially in the acute pulmonary failure, is becoming more and more important. Critically ill patients with severe pulmonary distress, characterized by respiratory insufficiency with severe hypoxemia and hypercapnia, often require invasive ventilatory support. Mechanical ventilation forces lungs to work under unphysiologic positive pressure. This condition, even with protective respiratory settings (low tidal volumes), brings to variuous degrees of barotrauma, volutrauma and biotrauma [2]. In addition it increases the risk of lung injury, infection, atelectasis, muscle fatigue, remote organ failure [3, 4] and it is recognized to be a significant risk factor for mortality after LTx [5]. Most of the patients, despite maximal mechanical ventilatory support, develop refractory hypercapnia and acidosis that require additional extracorporeal gas exchange.

Alternatively to the extracorporeal membrane oxigenation (ECMO), widely used until now, new devices such as the interventional lung assist NovaLung (iLA; NovaLung GmbH, Hecnigen, Germany) and the decapneization system Decap® [6, 7] have been applied. ILA is a low resistance lung assist device driven by the cardiac output that does not require extracorporeal pump assistance, it provides veno-arterious passive carbon dioxide removal by a diffusion membrane. On the contrary the Decap® system allows veno-venous extra-corporeal CO2 removal with a mini-invasive pump driven easy-to-use technique.

In this manuscript we report our experience with both the devices as bridge to transplant in patients on waiting list for LTx, with severe and unresponsive pulmonary failure.

Materials and Methods

At our institution from November 2005 to September 2009, 12 patients (7 males, 5 females, mean age 43.3 ± 15.5 years), on waiting list for lung transplantation, have been treated with extracorporeal devices for CO2 removal because of a severe ventilation-refractory hypercapnia and respiratory acidosis. In 6 patients a Decap® system was used, the remaining 6 patients underwent iLA

implantation. The decision on what device to use was made on the base of the hemodynamic capability of the patient to sustain extracorporeal gas exchange with or without the interposition of a centrifugal pump. Patients with an adequate mean arterial pressure to drive blood through the system have been treated with pumpless apparatus (iLA), those, supposed not to be able to sustain an extracorporeal gas exchange, have been supported with a Decap® device. No statistical difference was found in terms of patient characteristics between the two groups (data not shown).

Novalung has been implanted with the standard technique [8]. For the Decap® system, cannulation consisted in the insertion of a percutaneous single access with a double lumen catheter connected to a veno-venous circuit drived with a low flow pump (< 40 ml/min). A bolus of 5000 UI of heparin was administered intravenously followed by titrated administration to maintain the active clotting time value between 150 and 200. Administration of fluids, as well as vasopression or inotropic agents was targeted to maintain a mean arterial pressure (MAP) of 65 mm Hg [6, 7]. Perfusion of the lower extremities has been checked every day with Doppler examination.

In all patients arterial blood gas samples were taken at the moment of the implantation, 24, 48, 72 hours and 7 days after implantation.

Statistical Analysis

Data are presented as mean±SD, median (range) or frequencies (percent). Patients's characteristics of the femoral and direct aortic cannulation groups were compared with Student's *t*-test. Statistical significance was accepted for *P* values <0.05.

Results

All patients except one were on mechanical ventilatory support before the implant of the devices. The indication for decapneization device implantation was severe hypercapnia and acidosis refractory to positive high pressure mechanical ventilation. The only one not on ventilator was a lung transplanted patient treated with iLA because of a respiratory failure due to worsening of chronic rejection. This patient has been on iLA assistance, not intubated until lung re-transplantation. The diseases were: cystic fibrosis (6 pts), pulmonary emphysema (5 pts) and one case of chronic rejection in a previous double lung transplantation (table 1). The global mean duration on decapneization support was 13.5 ± 14.2 days (median 7.5, range 4 – 48 days), no statistical difference has been observed between iLA and Decap®. Pre and post implant changes in blood gases are shown in figure 1. There was s significant reduction in PaCO2 levels at 24, 48 and 72 hours post implant for both the extracorporeal systems used. No statistical difference was found at each time point in terms of PaO2 levels either pre versus post device implantation or iLA versus Decap® system. In only one case, because of thrombosis of the iLA a membrane replacement was required while cannulas were left in place. Only one patient was firstly weaned from ventilator and later from the Deca®p for a total period on device of 11 days. This patient is still on waiting list for double lung transplantation. Three patients (25%) has been successfully transplanted while the remaining eight died under decapneization treatment. Causes of death are summarized in table 2.

Discussion

The aim of percutaneous extracorporeal lung assistance devices insertion is to allow lung protective ventilation improving gas exchange and reducing, at the same time, high pressure-high volume mechanical ventilation lung damage. In this way, native lung function is supported and the diseased lung may better and quickly recover from the acute respiratory failure as artificial ventilation can be downregraded. Our results confirm the decapneization efficacy of iLA and Decap® at 24, 48 and 72 hours

post implantation of such devices in patients on waiting list for lung transplantation with acute respiratory failure refractory to mechanical high pressure ventilator support. No difference of PaCO2 post versus pre implantation has been observed, for both the devices, after seven days of extracorporeal CO2 removal. This data has to be critically analyzed taking into account that 50% of the patients were affected by cystic fibrosis and in 6 over 12 patients the duration of extracorporeal support has been lower than 7 days (3 underwent lung transplantation and 3 died on device because of severe pseudomonas pneumonia). No improvements in blood oxygenation has been found after the devices implantation. This evidence correlates with the purpose and design of both the systems used.

In our experience, the decision on what device to be used was made on the base of the emodinamic conditions. In patients with an adequate mean arterial pressure we used pumpless apparatus (iLA), while in the others we preferred a Decap® device. Thus, hemodynamic judgment before insertion of such devices is mandatory. For that purpose an echocardiographic evaluation to assess myocardial function and to estimate cardiac index has to be performed. In alternative, when possible, a Swan-Ganz catheterization may be beneficial in order to define which assistance to use.

We found no differences between the two extracorporeal assistances, this finding permitted us to extend the indication of extracorporeal decapneization also to those patients that previously would have been treated with ECMO and/or with high-pressure mechanical ventilation, two conditions that are widely recognized to negatively affect lung transplantation outcomes. Moreover ECMO brings to various side-effects such as infections, renal insufficiency, haemolysis and bleeding complications [9]. On the other hand invasive high pressure mechanical ventilation is responsible for different forms of lung damage like barotaruma , volutrauma, biochemical trauma and athelectrauma (ventilator associated lung injuries-VALI) [2, 10, 11]. In severe cases mechanical ventilation under high volume and positive pressure is an additional option it is well known to be a risk factor for pot-LTx mortality[5, 10, 11] and should be avoided under such circumstances if possible.

The above mentioned decapneization systems are clearly efficient in case of severe hypercapnia but with mild to moderate hypoxia. Veno-arterious ECMO remains the only solution for severely hypoxic patients.

In conclusion the extracorporeal assistance devices used in our center are clearly efficient and safe methods to support patients with deteriorating gas exchange avoiding any further ventilation-induced lung injury. Elimination of carbon dioxide is more effective than oxygenation. Thus, indications for these systems remain severe hypercapnia and respiratory acidosis with moderate hypoxia especially as bridge to transplant and bridge to recovery in patients either in waiting list or with primary graft dysfunction. Pumpless assistances and low flow pump driven devices ensured similar results permitting us to extend the indications also to those patients previously only eligible for ECMO. The limited number of lung transplantations performed due to a restriction of available lung donors still remains the major problem in particular for patients assisted with the above mentioned devices.

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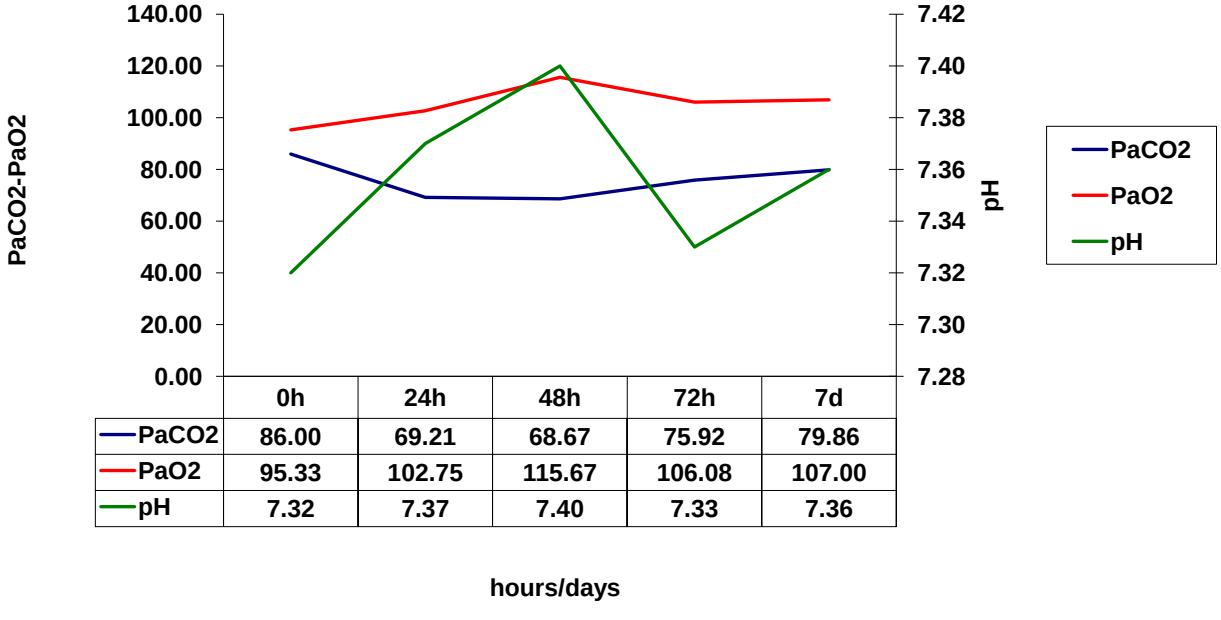
Table 1. Patients' characteristics (N= 12)	
Age	43.3 ± 15.6 years
Male	7 pts (58.3%)
Etiology	
Cystic Fibrosis	6 pts (50%)
Pulmonary Emphysema	5 pts (41.7%)
Chronic Rejection in previous LTx	1 pt (8.3%)
Treatment	
iLA	6 pts (50%)
Decap®	6 pts (50%)

Table 2. Patients' outcomes (N=12)	
Mean time of decapneization	13.5 ± 14.2 days
iLA	20.5 ± 17.9 days
Decap®	6.7 ± 2.7 days
	p=0.12
Death	8 pts (66.7%)
iLA	4 pts (33.3%)
Decap®	4 pts (33.3%)
Causes of death	
Pneumonia	5 pts (62.5%)
iLA	2 pts (40%)
Decap®	3 pts (60%)
Acute Respiratory Insufficiency	2 pts (25%)
iLA	1 pt (50%)
Decap®	1 pt (50%)
Multi Organ Failure	1 pt (12.5%)
iLA	1 pt (100%)
Decap®	0 pt
LTx	3 pts (25%)
Recovery (waiting list for LTx)	1 pt (8.33%)

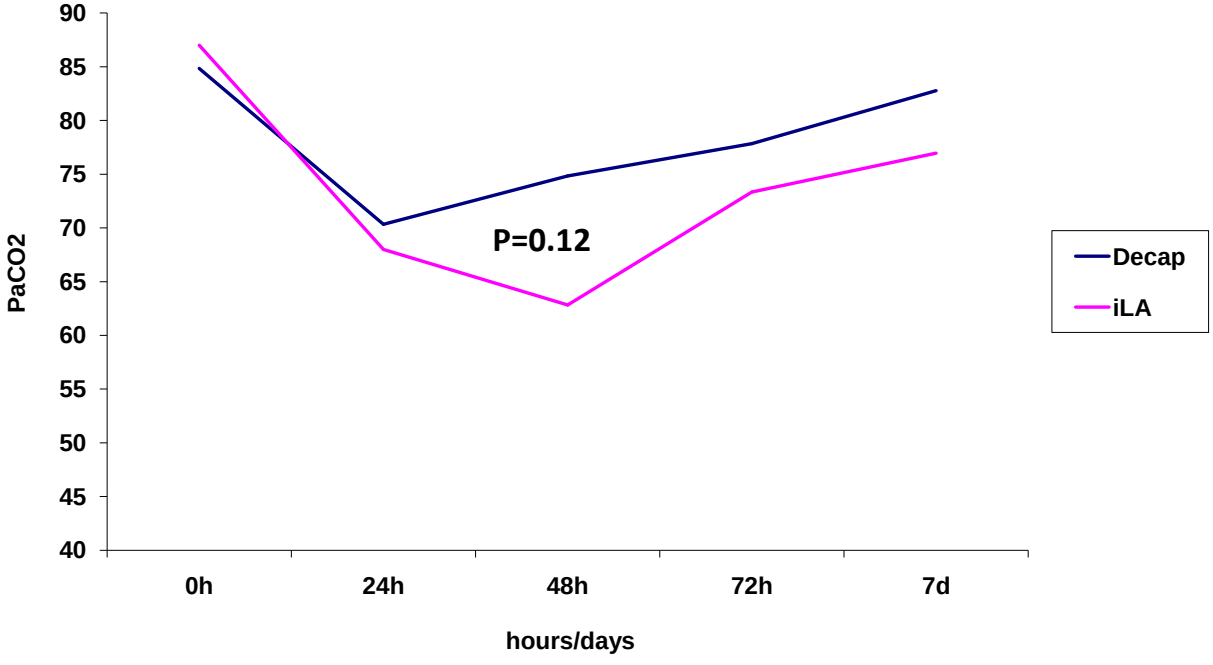
Figure 1. Changes in blood gases



	0h	24h	48h	72h	7d
PaCO2	86.00	69.21	68.67	75.92	79.86
PaO2	95.33	102.75	115.67	106.08	107.00
pH	7.32	7.37	7.40	7.33	7.36

	0h-24h	0h-48h	0h-72h	0h-7d
PaCO2	p=0.0016	p=0.012	p=0.039	p=0.33

Figure 2. Comparison between iLA and Decap ($PaCO_2$)


90
85
80
75
70
65
60
55
50
45
40
PaCO2
P=0.12
0h
24h
48h
72h
7d
hours/days
Decap
iLA